

### Remarks

Claims 1-3 and 22-30 are pending in the application. Claims 4-9 have been previously cancelled. Claims 10 and 18-21 have been cancelled. Claims 11-17 have been withdrawn as a result of an earlier restriction requirement. Claims 22-30 have been added. No new matter has been entered by way of the present amendment.

Regarding the rejection of claims 1-3, 7, 10 and 18-21 for an alleged scope of enablement deficiency, reconsideration by the Examiner is respectfully requested based on the following grounds. Claim 1 has been amended to be directed toward a *Thermococcus litteralis* DNA polymerase, thus overcoming the rejection based on the use of a Taq polymerase. Moreover, claim 1 has been amended so as to specify that the DNA template is "of between 50 and 50 000 base pair", based on the support found in paragraph [0046]. New claim 27 and dependent claims 28 to 30 are directed toward a method using a *Thermus aquaticus* DNA polymerase with a concentration of propanol ranging from 1% to 2.5%. Support for this amendment can be found in paragraph [0062] on pages 14-15.

Further regarding the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, the Examiner alleged that the combination of elements in claim 1 could be interpreted broadly so as to encompass elements that would result in a mutation rate of  $10^{-1}$ /bp/PCR, which would produce mutant libraries where no active genes are left according to the reference by Claveau *et al.* However, it is respectfully submitted that claim 1 as amended and limited to the Vent polymerase (*Thermococcus litteralis* DNA polymerase) with a maximal propanol concentration of 8% does not result in an error of  $10^{-1}$  but rather to a mutation rate of  $5.8 \times 10^{-3}$ , which corresponds to a mutation rate acceptable to obtain a biologically active protein. As well, new claim 27 is limited to the Taq polymerase with a maximal propanol concentration of 2.5% which also provides a mutation rate well under  $10^{-1}$ .

For purpose of clarity, claims 1 and 27 have been amended to state that the presence of propanol in the polymerization reaction is "in order to increase polymerase intrinsic capacity to induce random mutation".

Therefore, the removal of the rejection of claims 1-3, 7, 10 and 18-21 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claim rejections -- 35 U.S.C. § 103

Regarding the rejection of claims 1-3, 10 and 18-21 under 35 U.S.C. § 103(a) as allegedly being obvious in light of the references by Chevet *et al.* and Buchi, reconsideration by the Examiner is respectfully requested based on the following grounds. Substituting ethanol instead of propanol would lead to an unworkable embodiment. On page 791, left column, Claveau mentions that performing a PCR reaction involving a heating at 95°C, which allows for DNA denaturation, with ethanol "resulted in excessive evaporation". Contrary to ethanol, 1-propanol (having a boiling point over 95°C; see table 1 of Claveau *et al.*), can withstand heating at 95°C and act on the DNA polymerase. Paragraph [0048] on page 11 of the present application even states that 1-propanol was chosen for the present method because "its boiling point of 98°C which is superior to the denaturation temperature used in PCR (95°C)." Chevet *et al.* never teach nor suggest replacing ethanol with propanol, and in fact, Claveau *et al.* indicate that such a replacement is not recommended. It is therefore submitted that ethanol can not be considered as an equivalent by a person skilled in the art of PCR reaction, such substitution leading to unworkable embodiments. Removal of the rejection of claims 1-3, 10 and 18-21 under 35 U.S.C. § 103(a) is therefore respectfully requested.

Combined to the arguments and amendments presented hereinabove, it is submitted that claims 1-3, 10 and 18-21 are not obvious over the references Chevet *et al.* and Buchi.

New claims 22-26 and 28-30 have been added for purpose of clarity.

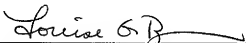
It is therefore submitted that the claims are in condition for allowance. Reconsideration of the Examiner's rejections is respectfully requested. Allowance of claims 1-3 and 22-30 at an early date is solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

A Request for Continued Examination is being filed concurrently. The Examiner is therefore requested to make entry of amendments and arguments presented herein.

A fee of 405\$ for small entity status is believed to be required in the filing of the present Request for Continued Examination. No other fees are believed to be required by the present response. However, should this be an error, authorization is hereby given to charge deposit account 19-5113 for any underpayment or to credit any overpayment.

Respectfully submitted,

  
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